

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
4 November 2004 (04.11.2004)

PCT

(10) International Publication Number  
**WO 2004/093852 A3**

(51) International Patent Classification<sup>7</sup>: **A61K 31/565**,  
31/568, A61P 9/00, 35/00, 11/06, 13/12

(21) International Application Number:  
PCT/GB2004/001663

(22) International Filing Date: 16 April 2004 (16.04.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
0308857.2 16 April 2003 (16.04.2003) GB

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(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

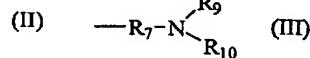
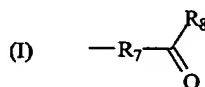
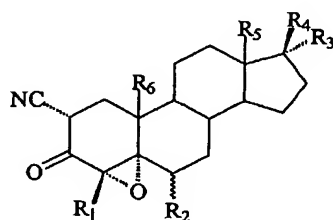
Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report:  
23 December 2004

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: USE OF STEROID DERIVATIVES FOR THE TREATMENT OF ANGIOTENSIN II RELATED DISEASE E.G. CARDIOVASCULAR AND PROLIFERATIVE DISORDERS



(III)

(57) Abstract: Use of a compound of formula (I) or a 3-enol C<sub>1 to 4</sub> alkanoyl ester thereof in the manufacture of a medicament for the treatment of an angiotensin II related disease in humans and animals wherein R<sub>1</sub>, R<sub>2</sub>, R<sub>5</sub>, R<sub>6</sub> are the same or different and each is hydrogen or C<sub>1 to 4</sub> alkyl; R<sub>3</sub> is hydrogen, C<sub>1 to 4</sub> alkyl, C<sub>2 to 4</sub> alkenyl or C<sub>2 to 4</sub> alkynyl; R<sub>4</sub> is hydroxyl, C<sub>1 to 4</sub> alkanoyloxy, a group of formula (II) or (III) wherein R<sub>7</sub> is (CH<sub>2</sub>)<sub>n</sub>, where n is an integer of from 0 to 4, R<sub>8</sub> is hydrogen, C<sub>1 to 4</sub> alkyl, hydroxy or NH<sub>2</sub> and R<sub>9</sub> and R<sub>10</sub> are the same or different and each is hydrogen or C<sub>1 to 4</sub> alkyl; or R<sub>3</sub> and R<sub>4</sub> together are oxo, ethylenedioxy or propylenedioxy.

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# INTERNATIONAL SEARCH REPORT

Int. Appl. No.  
PCT/GB2004/001663

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K31/565 A61K31/568 A61P9/00 A61P35/00 A61P11/06  
A61P13/12

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, EMBASE, PAJ, WPI Data, CHEM ABS Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2003/050291 A1 (ARAD YADON) 13 March 2003 (2003-03-13)	1-5, 7, 12, 13, 18-21, 29
Y	page 2, column 2, lines 4-7, 21, paragraph 2; claims 5, 6	6
X	GB 2 155 018 A (STERWIN AG) 18 September 1985 (1985-09-18)  page 2, lines 20, 21, 44-64 page 3, line 3	1, 2, 7, 8, 12-22, 28-31
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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*&\* document member of the same patent family

Date of the actual completion of the international search

23 July 2004

Date of mailing of the international search report

19/10/2004

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## INTERNATIONAL SEARCH REPORT

Int. Patent Application No  
PC1/GB2004/001663

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	SUZUKI GEORGE ET AL: "Effects of long-term monotherapy with eplerenone, a novel aldosterone blocker, on progression of left ventricular dysfunction and remodeling in dogs with heart failure." CIRCULATION, vol. 106, no. 23, 3 December 2002 (2002-12-03), pages 2967-2972, XP002288136 ISSN: 0009-7322 cited in the application page 2967, column 1, lines 6-8	1-11,29
Y	YAMAKADO M ET AL: "Sites of action of beta-melanocyte stimulating hormone in aldosterone biosynthesis in the rat." PROCEEDINGS OF THE SOCIETY FOR EXPERIMENTAL BIOLOGY AND MEDICINE. SOCIETY FOR EXPERIMENTAL BIOLOGY AND MEDICINE (NEW YORK, N. Y.) JUL 1985, vol. 179, no. 3, July 1985 (1985-07), pages 318-323, XP009033422 ISSN: 0037-9727 see abstract, l. 3-6 page 319, column 2, lines 20-27	1-11,29
Y	ROCHA RICARDO ET AL: "Selective aldosterone blockade prevents angiotensin II/salt-induced vascular inflammation in the rat heart." ENDOCRINOLOGY, vol. 143, no. 12, December 2002 (2002-12), pages 4828-4836, XP002288137 ISSN: 0013-7227 cited in the application page 4828, column 1, lines 14-22 page 4833, column 2, lines 1-33	22,25
Y	ROUSSEAU MICHEL F ET AL: "Beneficial neurohormonal profile of spironolactone in severe congestive heart failure: Results from the RALES neurohormonal substudy." JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY, vol. 40, no. 9, 6 November 2002 (2002-11-06), pages 1596-1601, XP002288138 ISSN: 0735-1097 page 1599, column 2, lines 1-7 see abstract page 1600, column 1, lines 1-5,20-31	22,25

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## INTERNATIONAL SEARCH REPORT

International Application No  
PC 1 / GB2004/001663

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	LEE A F ET AL: "Neurohormonal reactivation in heart failure patients on chronic ACE inhibitor therapy: a longitudinal study." EUROPEAN JOURNAL OF HEART FAILURE : JOURNAL OF THE WORKING GROUP ON HEART FAILURE OF THE EUROPEAN SOCIETY OF CARDIOLOGY. DEC 1999, vol. 1, no. 4, December 1999 (1999-12), pages 401-406, XP002288261 ISSN: 1388-9842 cited in the application abstract	22-24
A	EP 0 108 606 A (STERWIN AG) 16 May 1984 (1984-05-16) cited in the application page 2, lines 14-20 page 3, lines 1-5 page 5, lines 19-32	13-17

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/GB2004/001663

## Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 1, 2, 3, 7, 12-21, 29 and 30 (partially)  
because they relate to subject matter not required to be searched by this Authority, namely:  
Although claims 29-31 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.: 1, 2, 3, 7, 12-21, 29 and 30 (partially)  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

## Continuation of Box II.1

Although claims 29-31 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

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## Continuation of Box II.1

Claims Nos.: 1,2,3,7,12-21,29 and 30 (partially)

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

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## Continuation of Box II.2

Claims Nos.: 1,2,3,7,12-21,29 and 30 (partially)

Present claim 1 relates to the treatment of a disease which is not well defined. The use of the definition "angiotensin II related disease" in the present context is considered to lead to a lack of clarity within the meaning of Article 6 PCT. It is impossible to determine the diseases for which protection might legitimately be sought. The lack of clarity is such as to render a meaningful complete search impossible. Consequently, the search concerning the therapeutic application of the claimed compounds has been restricted to the diseases listed in claims 4-11.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB2004/001663

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
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